Applicant submits that the disclosed invention contains related processes and the apparatus for its practice. Group I describes the physical apparatus for making expression miniarrays – a novel category of biosensors devised by the inventor which are machine manufactured and intermediate in size, cost and ease of use between expensive, highly miniaturized, expression microarrays and common laboratory macroarrays which are typically hand-made one at a time. Microarrays generally contain thousands of gene probes and they are typically used to survey as many genes as possible in order to detect unknown or unpredicted gene effects, whereas the research-oriented macroarrays generally contain less than thirty gene probes and they are typically used to explore known or expected gene pathways. Most disease conditions such as the major cancers and inflammatory diseases only showed significant expression changes in 5 to 15 percent of the genes surveyed by high density microarrays. The present miniarrays can target limited subsets of 50 to 500 genes that are associated with or indicative of specific disease conditions, and furthermore, the present invention provides more specific features of array manufacture, organization and detection that facilitate that diagnostic function. Claims 1 to 22 describe the process and apparatus for forming the miniarrays and Claims 23 to 54 extend that process description more precisely in providing novel manufacturing arrangements of the gene probes and reagents employed in making and using the miniarrays for diagnostics. The apparatus and processes described in Claims 1 to 54 therefore all work together as a system

to achieve that integrated function. The sizing and clinical purpose of such intermediate minarrays dictates machine production and precludes hand manufacture.

MPEP 806.05(e) states that the burden is on the Examiner to provide reasonable examples that recite material differences between the apparatus and the process. Applicant submits that the Examiner's assertion of performing the claimed processes by hand is unreasonable. The Examiner's reasoning is analogous to stating that an apparatus for printing circuit boards for computers and the process of using that apparatus to print circuit boards are distinct because one could hand solder a circuit board. Even though one could pick up a high quality pipetter and attempt to duplicate the operation of machine manufacture, the resulting miniarrays would be crude and irregular and largely unsuitable for commercial sale or clinical use. Hand manufacture of multiple expression miniarrays as described in the subject invention wherein the miniarrays would contain hundreds of gene probes and would provide reliable consistent diagnostic data is unreasonable.

In view of the above remarks, Applicant submits that the Examiner has not provided reasonable examples that recite material differences between the apparatus and the process. The Examiner's assertion that the claimed processes could be performed by hand is not reasonable and it flies in the face of the value, purpose and operation of the subject invention. Applicant submits that the claims are not independent and are substantially connected in design,

operation, or effect under the disclosure of the particular application under consideration. Claims 1-6 recite the apparatus for forming the miniarrays; claims 7-22 describe the process of employing the apparatus to make these expression miniarrays and claims 23-54 further provide novel manufacturing arrangements of the gene probes and reagents employed in making and using the miniarrays towards diagnostic ends. Accordingly, Applicant requests that the proposed restriction be reconsidered and claims 1-54 be rejoined for examination.

Respectfully submitted,

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